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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,839	03/01/2000	RAJA G. ACHARI	719-75-PCT/U	4232

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[REDACTED] EXAMINER

JIANG, SHAOJIA A

[REDACTED] ART UNIT 1617 PAPER NUMBER

DATE MAILED: 04/09/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/486,839	ACHARI ET AL.
Examiner	Art Unit	
Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 23 January 2003.

2a)  This action is **FINAL**.                    2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## **Disposition of Claims**

4)  Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1-22 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)  All b)  Some \* c)  None of:

1.  Certified copies of the priority documents have been received.
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)  The translation of the foreign language provisional application has been received.

15)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)      4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_ .  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)      5)  Notice of Informal Patent Application (PTO-152)  
3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_ .      6)  Other: \_\_\_\_\_

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 23, 2003 has been entered in Paper No. 13.

This Office Action is a response to Applicant's request for continued examination (RCE) filed January 23, 2003 in Paper No. 13, and amendment and response to the Final Office Action (mailed April 9, 2002), filed January 23, 2003 in Paper No. 14 wherein claims 7 and 14-21 have been amended, and claim 22 is newly submitted. Currently, claims 1-22 are pending in this application.

Claims 1-22 are examined on the merits herein.

Applicant's amendment (amending claims 7 and 14-21) filed on January 23, 2003 in Paper No. 14 with respect to the rejection of claims 7, 14, 17-18, and 21 made under 35 U.S.C. 112 second paragraph for the use of the indefinite expressions, i.e., "a chemically modified equivalent" or "chemically modified equivalents" of record stated in the Office Action dated April 9, 2002 have been fully considered and found persuasive to remove the rejection since these expression has been removed from the claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith (WO 83/00286, of record) in view of JOSHI et al. (5,252,318, PTO-982) and *Handbook of Pharmaceutical Excipients*, 2<sup>nd</sup> Ed, page 383 (provided by Applicant in the response in Paper No. 14).

Keith discloses that an intranasal formulation comprising scopolamine hydrochloride in a pharmaceutically acceptable carrier, an aqueous solution containing ethanol, an aerosol spray vehicle, is useful in a method of preventing and/or treating motion sickness such as nausea and/or vomiting. See abstract, Examples I-XII, and claims 1-6. Keith also discloses that the intranasal formulation therein provides quick relief from motion sickness and the onset of effect is within ten minutes. See page 2 lines 3-4, page 3 Example II, and page 4 Example IV.

The prior art does not expressly disclose that the pH value of the instant intranasal formulation is below about 4 or 3.5, and the concentration of the buffer salt in the instant intranasal formulation is below about 200 mM or 100 mM or 50 mM. The prior art does also not expressly disclose the employment of polyvinyl alcohol in the formulation in combination with one or more additional gelling agents or bioadhesives such as alginates, gums, and starches in the instant intranasal formulation and method

for the treatment of motion sickness. The prior art does not further expressly disclose the employment of thickening agents and surfactants in the formulation herein. The prior art does not further expressly disclose that the instant intranasal formulation effects within about 5 minutes.

*Handbook of Pharmaceutical Excipients* teaches polyvinyl alcohol is a known viscosity increasing agent (also known as a thickening agent) and a known lubricant (page 383).

Joshi et al. discloses that drug delivery systems such as gelling aqueous compositions therein undergo significant changes in viscosity in response to substantially changes in pH and temperature (see abstract). Joshi et al. also teaches that by adjusting or controlling the pH of these drug delivery systems in an aqueous base through the addition of buffering agents, the viscosities of the compositions or formulations may be various (see col.1 lines 6-15, and col.2 lines 1-5 and 21-28). Joshi et al. also discloses that compositions or formulations therein exhibit steady state flow characteristics at or near room temperature at a pH range of 2.5 to 6.5, i.e., a pH of between 3.0 and 5.0 (see col.3 lines 33-35, and col.7-8 especially lines 57-59). Joshi et al. discloses the employment of lubricants such as polyvinyl alcohol (see col.12 lines 21-22) in combination with one or more additional gelling agents or bioadhesives in the formulations (see col.3 lines 24-48). Joshi et al. further discloses that the most promising drugs for incorporating into the aqueous drug delivery compositions therein include scopolamine (see col.11 lines 32-33).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to optimize the pH of the intranasal formulation herein to below about 4 or 3.5 and the concentration of the buffer salt in the instant intranasal formulation to below about 200 mM or 100 mM or 50 mM, to employ polyvinyl alcohol in combination with one or more additional gelling agents or bioadhesives in the instant intranasal formulation and method for the treatment of nausea and/or vomiting associated with motion sickness, and to further employ thickening agents and surfactants in the formulation herein.

One having ordinary skill in the art at the time the invention was made would have been motivated to optimize the pH of the instant intranasal formulation to below about 4 or 3.5 and the concentration of the buffer salt in the instant intranasal formulation to below about 200 mM or 100 mM or 50 mM, since gelling aqueous compositions in drug delivery systems are known to significantly change in viscosity in response to changes in pH and temperature according to Joshi et al. Joshi et al. also teaches that by adjusting or controlling the pH of these drug delivery systems in an aqueous base through the addition of buffering agents, the viscosities of the compositions or formulations may be various. Gelling aqueous compositions or formulations therein are known to exhibit steady state flow characteristics at or near room temperature at a pH range of 2.5 to 6.5, i.e., a pH of between 3.0 and 5.0 according to Joshi et al. Scopolamine is known to be one of the most promising drugs for incorporating into the aqueous drug delivery compositions of Joshi et al.

Therefore, one of ordinary skill in the art would find it obvious to optimize the pH by adjusting the concentration of buffering agents in order to make the formulations herein having optimized viscosities exhibiting steady state flow characteristics at or near room temperature since the optimization of parameters based on the known information, i.e., known pH range of 2.5 to 6.5, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980). Thus, Joshi et al. clearly provided the motivation and knowledge to optimize the pH and concentration of the buffering agents in the drug delivery system for scopolamine.

Moreover, one having ordinary skill in the art at the time the invention was made would have been motivated to employ polyvinyl alcohol in combination with one or more additional gelling agents or bioadhesives in the instant intranasal formulation and method for the treatment herein, and to further employ thickening agents and surfactants in the formulation herein, because the employment of lubricants such as polyvinyl alcohol in combination with one or more additional gelling agents or bioadhesives in the formulations and other thickening agents and surfactants are known to a skilled artisan according to Joshi et al.

It is noted that the instant intranasal formulation effecting within about 5 minutes is considered to be an inherent property of the formulation, which is not further limited the formulation.

Thus the claimed invention as a whole is clearly *prima facie* obvious over the combined teachings of the prior art.

Applicant's remarks filed on January 23, 2003 in Paper No. 14 with respect to the rejection of claims 1-21 made under 35 U.S.C. 103(a) as being unpatentable over Keith in view of Osol et al. for reasons of record stated in the Office Action dated April 9, 2002 have been fully considered but are moot in view of the new ground(s) of rejection set forth above.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.



S. Anna Jiang, Ph.D.  
Patent Examiner, AU 1617  
March 27, 2003